REMARKS

Applicants respectfully request reconsideration and allowance of the present claims in view of the foregoing amendments and reasons that follow.

The specification has been amended to correct an obvious typographical error in Scheme 8. Reaction of deazapurine 118 with bromide 103 results in displacement of the bromine atom to form the nucleoside 123. However, the bromine atom still appears in the drawings of structures 123, 124, 125, and 13; these errors have been corrected by this amendment. The abstract has also been modified to conform with MPEP 608.01(b).

Claims 1-2, 5-6, and 8-10 are pending in this application. Claim 1 has been amended by incorporating the W groups from claim 2, removing the term "and a pharmaceutically acceptable prodrug", incorporating the substituent formyl from dependent claim 8 into the definition of Z, and further limiting the list of Z substituents to formyl, halo, $-B(OH)_2$, nitro, alkenyl, substituted alkenyl, acetylenyl and substituted acetylenyl of the formula $-C\equiv C-R^4$. The same changes have also been made to Claim 5. Claims 2 and 6 are directed to compounds where W is hydrogen. Claim 8 has been amended to depend from claims 1 and 5 and to correct a typographical error in the spelling of the term "bromo." Claim 9 has been amended to correct a formatting errors (extraneous spaces) in the names of compounds 7 and 13. The names of compounds 12 and 17 have also been deleted from Claim 9. Claims 3-4, 7, and 11-12 have been canceled without prejudice. Applicants reserve the right to pursue the subject matter of these claims in a later filed continuation application.

Incorporation by Reference

The Examiner has objected to the specification as improperly incorporation by reference the foreign patents and non-patent publications listed on page 2, lines 8-10. The MPEP at section 608.01(p) provides that the incorporation of *essential material* in the specification by reference to a foreign application or patent, or to a publication is improper and that the applicants are required

to amend the disclosure to include the material incorporated by reference. The MPEP at the same section defines "essential material" as material necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112). "Nonessential" subject matter is subject matter referred to for purposes of indicating the background of the invention or illustrating the state of the art. Nonessential subject matter may be incorporated by reference to (1) patents or applications published by the United States or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications, or (3) non-patent publications.

References 1-5 referred to by the Examiner (listed on page 1 of the specification as filed, paragraphs [0004]-[0008] of the publication of the present application) are cited in the State of the Art section of the application and provide information regarding the current state of the art of understanding and treating HCV infections. As such, each of these references supply nonessential subject matter and are properly incorporated by reference.

Reference 5, Sommadossi, et al, and reference 6 , Carroll *et al.*, WO 02/057425, are cited at paragraph [0117] of the publication of the application as indicating the state of the art with regards to 2'-C-substituted sugars. Carroll, *et al*, is also cited at paragraph [0128] as indicating the state of the art with regards to preparation of known intermediate 115. The references provide examples as to the state of the art with regard to synthesis of various known intermediates or starting materials and as such provide nonessential material. References 5 and 6 are properly incorporated by reference.

Similarly, reference 7, Seela, is cited at paragraph [0120] of the application for describing a method of halogenation. Such methods are know in the art. As such, reference 7 provides an example of the state of the art of halogenation and is a properly incorporated nonessential reference.

The Examiner also makes reference to the improper incorporation by reference of U.S. patents but does not provide guidance as to the actual citation of the references. Applicants

assume this statement is in furtherance of the Examiner's objection to incorporation of the references cited on page 1 and had thus been adequately addressed above.

Claim Rejections – 35 U.S.C. §112, first paragraph

Claims 1-12 were rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one of ordinary skill in the art to make and/or use the invention.

Applicants have canceled claims 3-4, 7, and 11-12 in the interest of expediting prosecution.

Applicants respectfully traverse the rejection as it applies to pending claims 1-2, 5-6, and 8-10. These claims are directed toward compounds of Formula I or II and pharmaceutical compositions comprising the compounds. The Examiner has provided an analysis of the *In re Wands* factors used to determine if an invention can be practiced without undue experimentation. Specifically, the Examiner states that the level of one of ordinary skill in the art is high with regards to making of the compounds and pharmaceutical compositions as claimed in claims 1-10. The Examiner also states that the level of predictability in the art is elevated in the area of synthesis of the compounds. Importantly, as noted by the Examiner, the specification provides a high level of direction in the area of synthesis of the claimed compounds as well as providing working examples teaching synthesis of several of the compounds.

Applicants submit that pending claims 1-2, 5-6, and 8-10 are enabled and satisfy the requirements of 35 U.S.C. §112, first paragraph. Removal of this rejection is respectfully requested.

However, in the rejection under paragraph H of 35 U.S.C. §112, first paragraph, the Examiner objects to various terms in the compound claims as being excessively broad and indefinite thereby requiring undue experimentation. Applicants respectfully traverse the rejection

as the terms in the amended claims are neither broad nor indefinite for the reasons discussed below in relation to the 35 U.S.C. §112, second paragraph rejection of claims 1 and 5.

Claim Rejections – 35 U.S.C. §112, second paragraph

Claims 1-6, 9, and 11 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and claim the subject matter which the Applicants regard as the invention.

Claims 1 and 5 were rejected for use of the term "and a pharmaceutically acceptable prodrug". The term has been removed from claims 1 and 5.

Claims 1 and 5 were also rejected for use of the terms "alkyl," "substituted alkyl," "alkenyl," "substituted alkenyl," "alkynyl," "substituted alkynyl," "thioalkyl," "substituted amino," "acyl," "carboxyl ester," "substituted phenyl," "heteroaryl," "substituted heteroaryl," "heterocyclic or substituted heterocyclic group," "aryl," and "substituted aryl." The terms are alleged to be indefinite because 1) the substituted groups are not specified in the claim, 2) the upper size limit or range of the groups are not specified in the claim, or 3) the identity or location of the heteroatoms have not been specified.

This rejection is respectfully traversed. The terms "acyl" and "carboxy ester" do not appear in the amended claims. Definitions of the remaining terms are found in the specification and address the nature and number of the substituted groups or heteroatoms:

> "Alkyl" refers to alkyl groups having from 1 to 5 carbon atoms and more preferably 1 to 3 carbon atoms. The alkyl group may contain linear or branched carbon chains. This term is exemplified by groups such as methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *t*-butyl, *n*-pentyl and the like. The term C_1-C_2 alkyl refers to an alkyl group having one or two carbon atoms.
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> "Substituted alkyl" refers to an alkyl group having from 1 to 3, and preferably 1 to 2, substituents selected from the group consisting of alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxyl, nitro, carboxyl, carboxyl esters, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic.
>
> "Alkenyl" refers to alkenyl group preferably having from 2 to 6 carbon atoms and more preferably 2 to 4 carbon atoms and having at least 1 and preferably from

1-2 sites of alkenyl unsaturation. Such groups are exemplified by vinyl, allyl, but-3-en-1-yl, and the like.

"Substituted alkenyl" refers to alkenyl groups having from 1 to 3 substituents, and preferably 1 to 2 substituents, selected from the group consisting of alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxyl, nitro, carboxyl, carboxyl esters, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic with the proviso that any hydroxyl substitution is not attached to a vinyl (unsaturated) carbon atom.

"Alkynyl" refers to alkynyl group preferably having from 2 to 6 carbon atoms and more preferably 2 to 3 carbon atoms and having at least 1 and preferably from 1-2 sites of alkynyl unsaturation. A preferred alkynyl is C_2 alkynyl which is sometimes referred to herein as acetylenyl: -C≡CH.

"Substituted alkynyl" refers to alkynyl groups having from 1 to 3 substituents, and preferably 1 to 2 substituents, selected from the group consisting of alkoxy, substituted alkoxy, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cyano, halogen, hydroxyl, nitro, carboxyl, carboxyl esters, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, and substituted heterocyclic. A preferred substituted alkynyl is substituted acetylenyl which can be represented by the formula: -C≡CR^4 where R^4 is as defined herein.

"Thioalkyl" or "alkylthioether" or "thioalkoxy" refers to the group -S-alkyl.

"Substituted amino" refers to the group –NR′R″ where R′ and R″ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and where R′ and R″ are joined, together with the nitrogen bound thereto to form a heterocyclic or substituted heterocylic group provided that R′ and R″ are both not hydrogen. When R′ is hydrogen and R″ is alkyl, the substituted amino group is sometimes referred to herein as alkylamino. When R′ and R″ are alkyl, the substituted amino group is sometimes referred to herein as dialkylamino.

"Heteroaryl" refers to an aromatic group of from 1 to 10 carbon atoms and 1 to 4 heteroatoms selected from the group consisting of oxygen, nitrogen, sulfur, -S(O)-, and -$S(O)_2$- within the ring. Such heteroaryl groups can have a single ring (e.g., pyridyl or furyl) or multiple condensed rings (e.g., indolizinyl or benzothienyl) wherein the condensed rings may or may not be aromatic and/or contain a heteroatom provided that the point of attachment is through an atom of the aromatic heteroaryl group. Preferred heteroaryls include pyridyl, pyrrolyl, indolyl, thiophenyl, and furyl.

"Substituted heteroaryl" refers to heteroaryl groups that are substituted with from 1 to 3 substituents selected from the same group of substituents defined for substituted aryl.

"Heterocycle" or "heterocyclic" or "heterocycloalkyl" refers to a saturated or unsaturated, but not heteroaromatic, group having a single ring or multiple condensed rings, from 1 to 10 carbon atoms and from 1 to 4 hetero atoms selected from the group consisting of nitrogen,oxygen, sulfur, -S(O)- and $-S(O)_2-$ within the ring wherein, in fused ring systems, one or more the rings can be cycloalkyl, aryl or heteroaryl provided that the point of attachment is through the heterocyclic ring.

"Substituted heterocyclic" or "substituted heterocycloalkyl" refers to heterocycle groups that are substituted with from 1 to 3 of the same substituents as defined for substituted cycloalkyl.

"Aryl" or "Ar" refers to a monovalent aromatic carbocyclic group of from 6 to 14 carbon atoms having a single ring (e.g., phenyl) or multiple condensed rings (e.g., naphthyl or anthryl) which condensed rings may or may not be aromatic (e.g., 2-benzoxazolinone, 2H-1,4-benzoxazin-3(4H)-one-7-yl, and the like) provided that the point of attachment is at an aromatic carbon atom. Preferred aryls include phenyl and naphthyl.

"Substituted aryl" refers to aryl groups including phenyl groups (sometimes referred to herein as "substituted phenyl") which are substituted with from 1 to 3 substituents, and preferably 1 to 2 substituents, selected from the group consisting of hydroxy, acyl, acylamino, acyloxy, alkyl, substituted alkyl, alkoxy, substituted alkoxy, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, amino, substituted amino, aminoacyl, aryl, substituted aryl, aryloxy, substituted aryloxy, cycloalkoxy, substituted cycloalkoxy, carboxyl, carboxyl esters, cyano, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thioheteroaryl, substituted thioheteroaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheterocyclic, substituted thioheterocyclic, cycloalkyl, substituted cycloalkyl, halo, nitro, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, and substituted heterocyclyloxy.

The specification further elaborates on the nature of the substituents:

It is understood that in all substituted groups defined above, polymers arrived at by defining substituents with further substituents to themselves (e.g., substituted aryl having a substituted aryl group as a substituent which is itself substituted with a substituted aryl group, etc.) are not intended for inclusion herein. In such cases, the maximum number of such substituents is three. That is to say that each of the above definitions is constrained by a limitation that, for example, substituted aryl groups are limted to –substituted aryl-(substituted aryl)-substituted aryl.

Similarly, it is understood that the above definitions are not intended to include impermissible substitution patterns (e.g., methyl substituted with 5 fluoro groups or a hydroxyl group alpha to ethenylic or acetylenic unsaturation). Such impermissible substitution patterns are well known to the skilled artisan.

Applicants contend that the definitions provided in the application would allow one of skill in the art to reasonably discern the scope of the claims.

Claims 2, 3, 4, and 6 are objected to under 35 U.S.C. §112, second paragraph for lacking proper antecedent basis. Claim 4 is also objected to with respect to the term "acyl group derived from an amino acid." Claims 3 and 4 have been canceled. Claims 2 and 6 have been amended and are directed to compounds where W is hydrogen.

Claim 9 is objected to with respect to the term "carbaldehyde oxime" which corresponds to compound 12. This compound has been deleted from the claim.

Claim 9 is also objected to in relation for use of the term "boronic acid" as appearing to refer to a separate compound and for failing to define how the group is attached to the 7-deazapurine ring. Applicants note that the term applies to compound 13 and that its name "1-(6-hydroxylamino-7-(boronic acid)-7-deazapurin-9-yl)-2-methyl-β-D-ribofuranose (13)" is correlated with its structure in Table 1 of paragraph [0045]. The term boronic acid is a well recognized and unambiguous description of the group $-B(OH)_2$, and the applicants are not aware of any alternate names for this group. The term is further identified as "7-(boronic acid)" indicating that the boronic acid is not a separate compound but a substituent attached to the 7 position of the 7-deazapurine ring.

Claim 11 was rejected for use of the term "at least in part by a virus of the *flaviridae* family of viruses." This rejection no longer applies as the claim has been canceled.

Applicants respectfully request removal of the rejection under 35 U.S.C. §112, second paragraph as applied to claims 1-2, 5-6, and 9.

Claim Rejections – Obviousness-type double patenting

Claims 1-12 have been rejected under the judicially created doctrine of obviousness-type double patenting over co-pending U.S. application No. 10/676,956. Applicants respectfully request that this rejection by held in abeyance pending final determination of patentable subject matter.

Prior Art Rejection – 35 U.S.C. §102(e)

Claims 1-12 have been rejected under 35 U.S.C. §102(e) as being anticipated by Ribapharm (WO 03/061576). Claims 1 and 5 have been amended so that Z is limited to formyl, halo, $-B(OH)_2$, nitro, alkenyl, substituted alkenyl, acetylenyl and substituted acetylenyl of the formula $-C\equiv C-R^4$. Claims 1 and 5 are therefore no longer anticipated by the Ribapharm application. Claim 8 is also not anticipated by the Ribapharm application as its scope is consistent with amended claims 1 and 5. Claim 9 has been amended to remove compounds 12 and 17 which contain the respective Z groups -C(=NHOH)H and cyano. Claim 10 has a scope commensurate with that of amended claims 1, 5, and 9 from which it depends and therefore is also not anticipated. The remaining claims have been canceled. Applicants respectfully request removal of the rejection under 35 U.S.C. §102(e).

Applicants respectfully submit that all pending claims are allowable and that the application is in condition for allowance. If the Examiner believes a telephone conversation would help advance prosecution in this case, the Examiner is invited to contact the undersigned attorney at the number set out below.

Respectfully submitted,

Date 11-7-05

By _____

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